Kidney International, Vol. 42 (1992), pp. 292–299

Uninephrectomy enhances urolithiasis in ethylene glycol treated rats

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Uninephrectomy enhances urolithiasis in ethylene glycol treated rats. Uninephrectomy (uNX) usually induces compensatory hyperfunction of the remaining kidney in an attempt to preserve the homeostasis of body fluid composition. The present study used uninephrectomized Sprague-Dawley rats on a lithogenic diet (0.5% ethylene glycol, EG) to evaluate the influence on urinary stone formation and calcium oxalate crystal deposition of compensatory excretion of lithogenic substances in the remnant kidney. The results showed that there were no urinary stones or calcium oxalate crystal deposits in the intact or uNX rats fed a normal diet. In the EG feeding groups, the incidence of massive (grade 3) crystal deposits was significantly higher in the uNX rats (87.5%) than that in the intact rats (37.5%; $P < 0.05$). The incidence of urinary stone formation was also higher in the uNX rats as compared to that of the intact rats, although the difference did not achieve statistical significance. The serum magnesium, phosphorus and creatinine increased significantly, whereas creatinine clearance (C_{Cr}), 24-hour urinary excretions of citrate, sodium, potassium and chloride decreased significantly in the uNX rats fed EG. These data indicate that uninephrectomy increases the vulnerability of the contralateral remnant kidney to urolithiasis and crystal deposition when the lithogenic risk factors are present. Furthermore, once the remnant kidney forms urolithiasis or massive calcium oxalate crystal deposits, the renal function is severely compromised.

Functioning renal mass reduction due to surgical ablation or partial infarction usually induces morphological and functional hypertrophy in animals and humans [1–7]. The adaptive changes include hyperfiltration and hyperexcretion resulting from alterations in glomerular and peritubular hemodynamics and tubular transport processes [8, 9]. These compensatory adaptations in renal structure and function may have distinct physiological and pathological implications. On the one hand, the functional hypertrophy is beneficial in the sense that it minimizes the reduction of filtered load and solute and water excretion that would otherwise occur following uninephrectomy. Thus, hyperfiltration and hyperexcretion serve to preserve the homeostasis of body fluid composition. On the other hand, compensatory hypertrophy in the renal structure and function may eventually induce pathological processes leading to sclerotic lesions and glomerular dysfunction. Moreover, increased filtered load and excessive urinary excretion of lithogenic substances in the remaining nephron units may cause supersaturation of urine leading to crystallization and urolithiasis as postulated by the hyperexcretion-crystallization hypothesis [10, 11]. However, there is still no direct evidence indicating that the compensatory excretion of lithogenic substances in the remnant kidney after uninephrectomy will enhance urolithiasis. By using the ethylene glycol-induced urolithiasis animal model [12–16], the aim of this study was to determine if uninephrectomy could enhance urinary calculi formation. The results indicate that uninephrectomy increases the vulnerability of the remnant kidney to stone formation and crystal deposition when the lithogenic risk factors are present. This may have significant clinical implications, since some urolithiasis patients first seeking medical treatment may have already exhibited urinary calculi with ipsilateral renal damage. Regardless of whether the diseased kidney is left alone or may require surgical removal later, the remnant kidney may carry a higher risk of stone formation and is more vulnerable to further damage if it is exposed continuously to lithogenic factors.

Received for publication September 17, 1991
and in revised form March 2, 1992
Accepted for publication March 2, 1992

Methods

Experimental animals

Adult male Sprague-Dawley rats initially weighing 250 to 300 g were randomly divided into four groups: Group 1, seven rats fed AIN-76 semipurified diet containing 1.75% calcium phosphate dibasic (50 g/100 g diet), 0.26% sodium chloride (740 mg/100 g diet), 0.77% potassium citrate monohydrate (22 g/100 g diet), 0.08% magnesium oxide (240 mg/100 g diet), vitamin A 400,000 IU, vitamin D 100,000 IU, (ICN Biomedicals, Cleveland, Ohio, USA) and tap water *ad libitum* for four weeks; group 2, seven rats received uninephrectomy and were treated the same as that of group 1; group 3, eight rats fed AIN-76 semipurified diet and received 0.5% ethylene glycol (reagent grade, Merck, Darmstadt, Germany) in drinking water for four weeks; group 4, eight rats received uninephrectomy and were treated the same as that of group 3 two weeks later. All rats were housed individually in metabolism cages (Nalge, Rochester, New York, USA) in an animal room with the temperature maintained at 22°C.

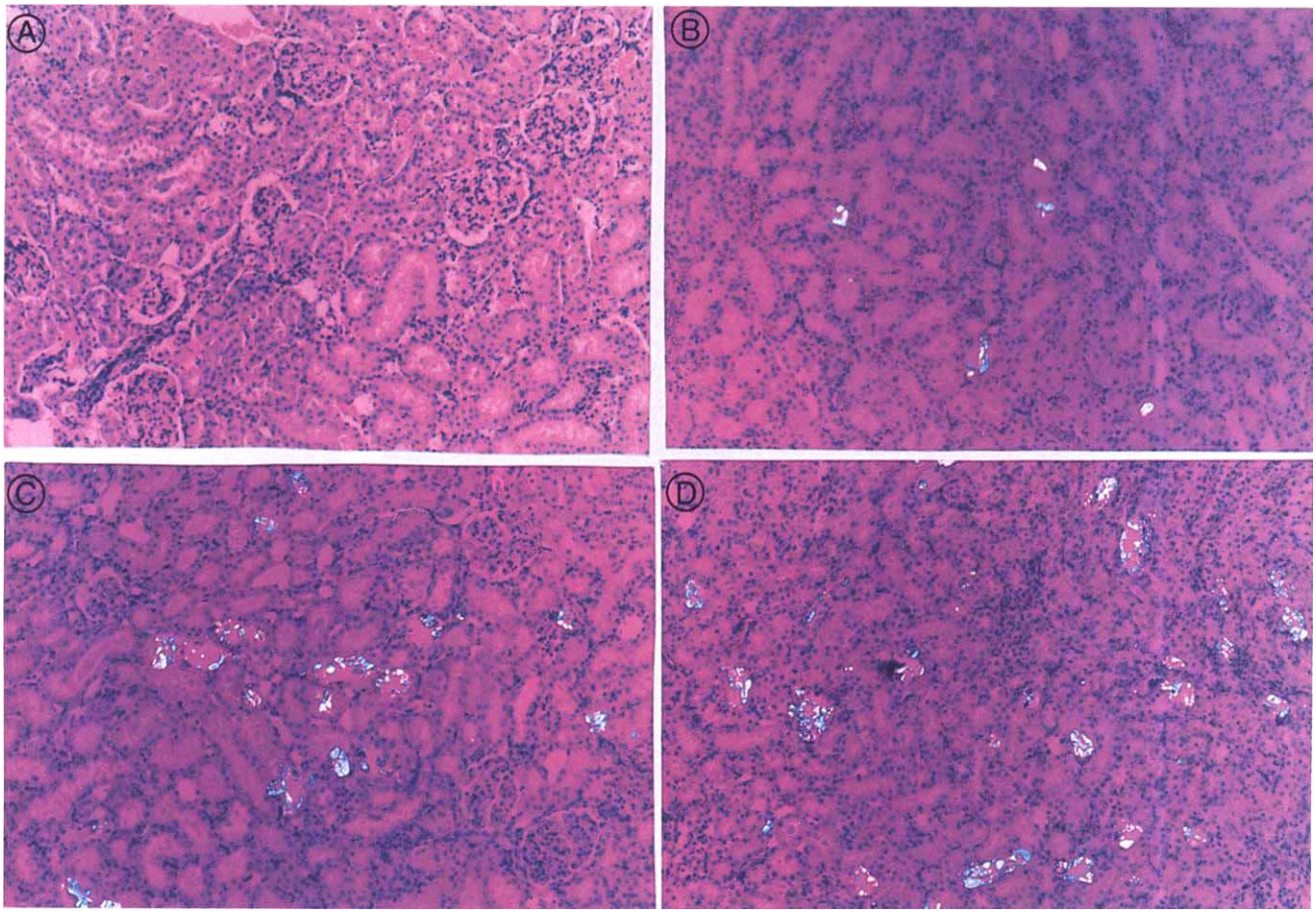

Fig. 1. *Grading of crystal deposition.* The section of kidney has been stained with hematoxylin and eosin and is being viewed by polarizing microscope (× 100). The birefringent spots seen in B-D are presumed to calcium oxalate crystals. The semi-quantitative grading of crystal deposition is: **(A)** nil (grade 0), **(B)** mild (grade 1), **(C)** moderate (grade 2), **(D)** massive (grade 3).

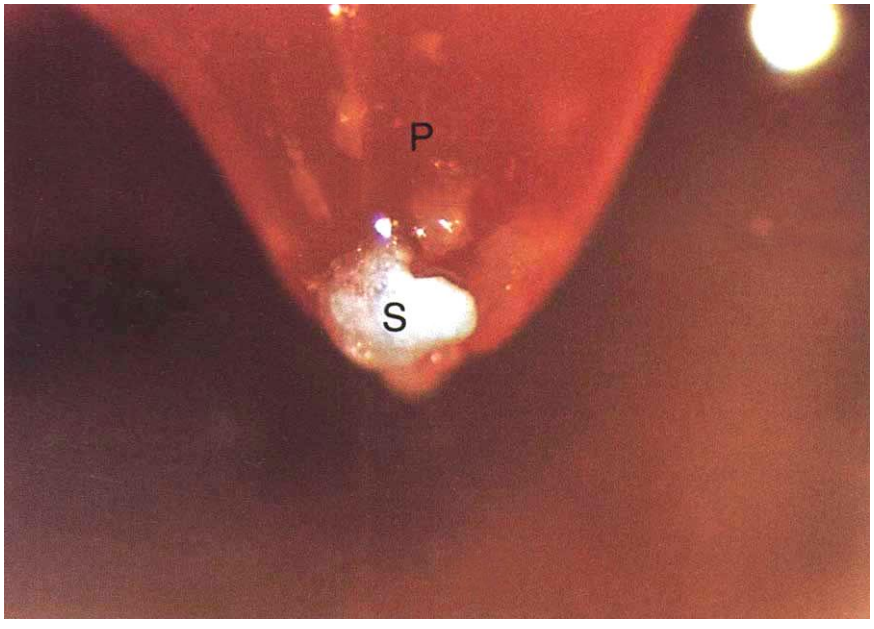

Fig. 5. *Stereo microscopic view of renal papilla (× 64) showing stones formed within the tip of renal papilla.* Abbreviations are: P, papilla; S, stone.

Table 1. The body weight, wet and dry kidney weight, and contents of calcium and magnesium in rats of different groups

Groups (*N*)	Body wt *g*		Kidney wt *g*		Wet kidney wt / Body wt × 100	Calcium	Magnesium
	Initial	Final	Wet	Dry		*μg/g dry tissue*	
Normal diet							
Intact (7)	309 (299–328)	459 (391–490)	1.38 (1.26–1.77)	0.31 (0.27–0.38)	0.32 (0.26–0.37)	250 (234–287)	570 (515–590)
uNX (7)	319 (301–324)	452 (398–496)	1.86 (1.64–2.10)	0.47 (0.45–0.54)	0.42 (0.39–0.53)	311 (211–386)	570 (555–592)
P	NS	NS	<0.01	<0.01	<0.01	NS	NS
EG diet							
Intact (8)	300 (286–324)	376 (338–430)	2.25 (1.27–3.99)	0.49 (0.31–0.84)	0.61 (0.33–1.18)	28900 (256–49938)	570 (510–755)
uNX (8)	320 (300–330)	372 (310–465)	4.16 (1.89–4.59)	0.94 (0.49–1.24)	1.06 (0.44–1.41)	88600 (1332–108150)	680 (515–1045)
P	NS	NS	<0.05	<0.05	<0.05	<0.01	NS
Normal diet vs. EG diet							
Intact	NS	<0.05	<0.05	<0.05	<0.01	<0.01	NS
uNX	NS	<0.05	<0.01	<0.01	<0.01	<0.01	NS

Abbreviations: N, number of rats; EG, ethylene glycol; uNX, uninephrectomy; NS, not significant.

Surgical preparations

For uninephrectomy, rats were anesthetized with sodium pentobarbital (50 mg/kg body wt, i.p.). A small incision was made over the left flank area, and the left kidney was removed after careful ligation of the renal vessels and ureter. After surgery all uninephrectomized rats were given penicillin (50,000 U, i.m.) once a day for prophylaxis of wound infection.

Urine and blood sampling

Urine was collected over a 24-hour interval. The daily urine volume, pH, total excretion of oxalate, citrate, uric acid, calcium, magnesium, inorganic phosphate, sodium, potassium, chloride and creatinine were measured every other day.

On the day of sacrifice, rats were anesthetized with sodium pentobarbital (50 mg/kg body wt, i.p.) and 5 to 10 ml venous blood was withdrawn from the inferior vena cava for determinations of serum creatinine, calcium, magnesium, phosphorus, sodium, potassium and chloride.

Verification of urinary stone formation

The kidneys and urinary bladders of all rats were removed, cut longitudinally, and examined under a stereomicroscope (Olympus SZH model, Tokyo, Japan) for verifying urinary tract stone formation. The right kidneys of intact rats and one half of the right kidneys of the uninephrectomized rats were then fixed with formaldehyde for hematoxylin eosin stain. The crystal deposits were examined using an Olympus BH-2 polarizing microscope. The extent of crystal deposit was graded semi-quantitatively into four grades (0 to 3) ranging from "no crystal deposit to massive crystal deposit" (Fig. 1, A-D) as previously described [17–19]. The left kidneys of intact rats and the remaining half of the right kidneys of the uninephrectomized rats were dried for two days in a vacuum oven at 95°C in the presence of 12 N KOH. They were then ground into fine powder with a mortar and pestle, and dried again in a vacuum at 95°C overnight. One hundred milligrams of dried kidney tissue was dissolved in 1 ml 6 N HCl and the supernatant was separated for the determination of calcium and magnesium content. The characteristics of the stones were examined by scanning electron microscopy (Hitachi, model S-2100, Tokyo, Japan).

Table 2. Characteristics of renal calcium content, kidney weight, stone formation and crystal deposit in the uninephrectomized rats fed with EG

Rat no.	Calcium content *% DKW*	Total calcium content *mg*	Kidney weight *g*		Stone formation	Crystal deposit (grading)
			WKW	DKW		
1	9.83%	121.9	4.54	1.24	present	3
2	9.98%	113.8	4.50	1.14	present	3
3	10.82%	115.8	4.59	1.07	present	3
4	11.11%	105.5	4.32	0.95	present	3
5	10.26%	87.2	4.00	0.85	present	3
6	8.86%	65.6	3.31	0.74	absent	3
7	6.08%	38.9	3.78	0.64	absent	3
8	0.13%	0.64	1.89	0.49	absent	2

Abbreviations are: DKW, dried kidney weight; WKW, wet kidney weight.

Assays

Calcium and magnesium concentrations in plasma, urine and the kidney tissue were measured with an atomic absorption spectrophotometer (Instrumentation Laboratory Inc., Maryland, USA). The serum phosphorus and urinary inorganic phosphate levels were measured by a Paramax autoanalyzer (Baxter, California, USA). Urinary citrate was assayed by the enzymatic method (Boehringer Mannheim citrate assay kit, Mannheim, Germany) and urinary oxalate was determined by the oxalate oxidase enzymatic method with an oxalate assay kit (Sigma, St. Louis, Missouri, USA). The serum and urinary concentrations of sodium and potassium were measured by flame photometry (Eppendorf, model FCM 6341, Germany). The serum and urinary chloride levels were measured by ASTRA autoanalyzer (ASTRA 8, Beckman Instruments, Fullerton, California, USA), as were the creatinine concentrations in the serum and urine samples. Calculation of the creatinine clearance (C_{Cr}, ml/min) was based on the clearance equation:

Table 3. The final creatinine clearance (C_{Cr}) and serum concentrations of electrolytes and creatinine in four groups of rats with different treatments

Groups (*N*)	C_{Cr} *ml/min*	Ca	Mg	P	Na	K	Cl	Cr *mg/dl*
		mg/dl			*mEq/liter*			
Normal diet								
Intact (7)	1.33	10	1.8	7.0	143	4.2	109	0.5
	(1.01–1.56)	(9.6–10.1)	(1.7–2.2)	(5.6–8.1)	(141–145)	(4.0–4.5)	(108–111)	(0.5–0.5)
uNX (7)	1.62	10.3	2.1	6.8	143	4.5	109	0.5
	(0.89–1.85)	(10–11)	(1.9–2.3)	(5.3–8.5)	(142–145)	(3.9–4.8)	(108–111)	(0.5–0.5)
EG diet								
Intact (8)	0.94	10.2	2.4	9.1[a]	144	4.5	107	1.2[a]
	(0.45–1.33)	(9.5–10.7)	(1.8–3.1)	(6.7–10.8)	(141–146)	(4.1–4.9)	(102–112)	(0.5–3.2)
uNX (8)	0.63[a]	9.7	3.2[a]	25.6[a]	145	4.7	110	7.1[a]
	(0.08–1.12)	(9.5–10.9)	(1.9–5.9)	(9.2–59)	(142–147)	(4.1–5.0)	(105–120)	(0.5–10.9)

Abbreviations are: Ca, calcium; Mg, magnesium; P, phosphorus; Na, sodium; K, potassium; Cl, chloride; Cr, creatinine.
[a] $P < 0.05$

Table 4. Urine biochemistry

	Normal diet				EG diet			
	Intact		uNX		Intact		uNX	
	Initial	Final	Initial	Final	Initial	Final	Initial	Final
pH	6.44	6.58	6.61	6.56	6.37	7.41[a]	6.48	7.48[a]
	(5.53–7.92)	(5.82–8.31)	(5.59–8.58)	(5.67–8.15)	(5.56–7.81)	(5.91–8.89)	(5.82–7.14)	(5.86–8.94)
Oxalate *μM/24 hr*	3.92	3.53	3.32	3.98	2.99	28.4[b]	3.34	23.4[b]
	(1.54–4.61)	(1.47–4.81)	(1.61–4.73)	(1.82–5.24)	(1.82–4.53)	(7.15–45.2)	(1.25–6.18)	(8.51–52.1)
Citrate *μM/24 hr*	6.15	5.92	6.27	5.97	5.53	4.84	5.96	2.44[a]
	(2.89–9.53)	(2.91–9.45)	(2.84–8.87)	(2.76–8.54)	(2.53–9.72)	(1.66–8.83)	(2.75–8.94)	(0.88–3.93)
Uric acid *μM/24 hr*	6.78	7.20	6.37	6.73	6.79	5.89	5.54	6.07
	(4.41–10.48)	(3.93–9.35)	(4.29–10.06)	(3.45–9.17)	(3.99–8.27)	(3.33–8.75)	(3.81–9.17)	(3.93–9.88)
Calcium *μM/24 hr*	28.3	29.5	25.5	27.8	25.3	5.75[b]	28.0	4.01[b]
	(13.8–36.8)	(16.8–38.5)	(14.3–40.8)	(15.3–41.3)	(13.8–35.5)	(1.25–11.3)	(15.8–45.8)	(1.02–8.25)
Magnesium *μm/24 hr*	0.08	0.09	0.10	0.11	0.08	0.08	0.08	0.09
	(0.05–0.11)	(0.05–0.11)	(0.05–0.13)	(0.05–0.12)	(0.05–0.10)	(0.05–0.10)	(0.05–0.11)	(0.03–0.11)
Phosphate *μm/24 hr*	0.37	0.39	0.39	0.38	0.40	0.36	0.38	0.35
	(0.31–0.42)	(0.33–0.45)	(0.28–0.58)	(0.29–0.46)	(0.31–0.49)	(0.27–0.43)	(0.30–0.54)	(0.19–0.44)
Sodium *μm/24 hr*	0.74	0.73	0.71	0.69	0.66	0.57	0.78	0.43[a]
	(0.65–0.99)	(0.57–0.93)	(0.54–1.1)	(0.45–0.89)	(0.48–0.82)	(0.39–1.12)	(0.45–0.94)	(0.25–0.59)
Potassium *μm/24 hr*	1.37	1.37	1.38	1.36	1.31	0.93	1.25	0.88[a]
	(1.27–1.41)	(1.28–1.42)	(1.29–1.45)	(1.24–1.49)	(1.13–1.65)	(0.79–1.25)	(1.11–1.65)	(0.72–1.12)
Chloride *μm/24 hr*	0.71	0.73	0.78	0.72	0.65	0.52	0.73	0.31[a]
	(0.45–0.93)	(0.47–0.94)	(0.55–1.13)	(0.49–0.92)	(0.48–0.86)	(0.42–0.96)	(0.53–1.02)	(0.15–0.61)

[a] $P < 0.05$
[b] $P < 0.01$

$C_{Cr} = U_{Cr} \cdot \dot{V}/P_{Cr}$, where U_{Cr} and P_{Cr} denote urine and plasma concentration of creatinine (mg/dl), respectively, and $\dot{V}$ denotes urine flow (ml/min).

Statistics

The results are expressed as median and range. Data were evaluated using Mann-Whitney U test for random samples or paired differences. The incidence of stone formation and crystal deposit in rats fed with EG was evaluated using Fisher's exact test. A probability value less than 0.05 was considered significant.

Results

As shown in Table 1, the body weights of rats at the beginning of the study were not significantly different between the four groups. However, at the end of the study, the rats treated with 0.5% EG weighed less than those on the normal diet. The absolute wet and dry kidney weights and the wet kidney weight/body weight ratio were significantly greater in the uninephrectomized rats than in the intact rats. Similarly, greater increases in the corresponding kidney weight and the kidney/body weight ratio were noted in the uninephrectomized rats treated with 0.5% EG as compared to those of the intact rats. Ethylene glycol feeding markedly increased the calcium content of the dried kidneys in both the intact and the uninephrectomized rats, but the magnitude of increase was significantly greater in the latter group of rats. The magnesium content in the dried kidney was not discernibly different between the four groups. It must be pointed out that in the uninephrectomized rats fed EG, the calcium content of the dried kidney was strikingly high and exhibited considerable individual variation (0.13% to 11.11% of dried kidney tissue) as shown in Table 2. The high calcium content in the dry kidney is apparently correlated with the degree of renal hypertrophy, urinary stone

Table 5. The incidence of urinary stone formation and crystal deposit in rats fed with EG

	Intact rats (N = 8)	uNX rats (N = 8)
	No. (%)	
Stone formation	4 (50%)	5 (62.5%)
Crystal deposit		
Grade 0	2 (25%)	0 (0%)
1	1 (12.5%)	0 (0%)
2	2 (25%)	1 (12.5%)
3	3 (37.5%)	7 (87.5%)[a]

[a] $P < 0.05$

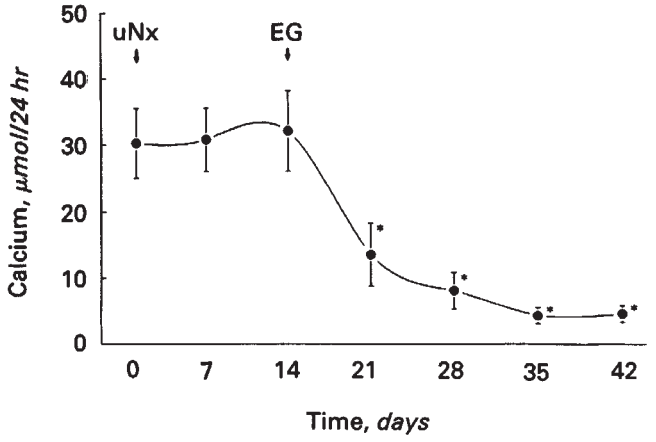

Fig. 2. *Changes in 24-hour urinary excretion of calcium in uninephrectomized rats fed ethylene glycol.* Abbreviations are: uNX, uninephrectomy; EG, 0.5% ethylene glycol; * $P < 0.05$.

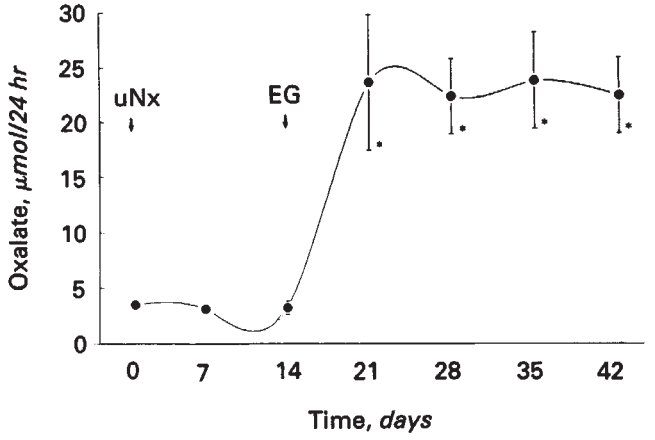

Fig. 3. *Changes in 24-hour urinary excretion of oxalate in the uninephrectomized rats fed ethylene glycol.* * $P < 0.05$.

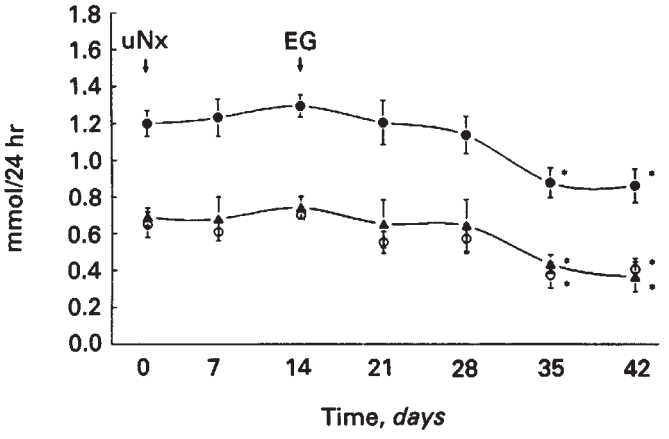

Fig. 4. *Changes in 24-hour urinary excretions of sodium, potassium and chloride in the uninephrectomized rats fed ethylene glycol.* * $P < 0.05$. Symbols are: (○) Na; (●) K, (▲) Cl.

formation and calcium oxalate crystal deposit in this group of rats.

The creatinine clearance (C_{Cr}) and serum biochemical data in four groups of rats with different treatments were measured on the day of sacrifice, and are shown in Table 3. Serum levels of magnesium, phosphorus and creatinine significantly increased, whereas C_{Cr} decreased markedly in the uninephrectomized rats fed 0.5% EG. However, in intact rats fed 0.5% EG only serum phosphorus increased. There were no significant differences in serum electrolytes, creatinine and C_{Cr} between the intact and the uninephrectomized rats fed the normal diet.

Table 4 summarizes the initial and the final urinary pH and 24-hour urinary excretion of oxalate, citrate, uric acid, calcium, magnesium, inorganic phosphate, sodium, potassium and chloride. There were no significant differences in the daily excretion of these solutes and urine pH between the intact and the uninephrectomized rats on the normal diet. When the intact and the uninephrectomized rats were fed 0.5% EG, the urinary pH and 24-hour urinary oxalate excretion increased, whereas the calcium excretion decreased significantly. The daily excretions of citrate, sodium, potassium and chloride decreased only in the uninephrectomized rats fed EG. The change of 24-hour urinary excretions of calcium, oxalate, sodium, potassium, and chloride over the time course in the uninephrectomized rats fed EG are depicted in Figures 2, 3, and 4. Uninephrectomy did not significantly alter the daily excretions of these solutes. However, after EG feeding, which commenced at 14th day, a profound increase in oxalate excretion and a decrease in calcium excretion were observed within one week and persisted throughout the experiment. The 24-hour urinary excretion of sodium, potassium and chloride decreased significantly until the third week of EG treatment and remained at the low level thereafter.

There were no urinary stones or calcium oxalate crystal deposits in the intact or the uninephrectomized rats fed the normal diet. The incidences of stone formation and crystal deposition in rats fed EG are listed in Table 5. The percentage incidence of urinary stone formation in EG-fed, uninephrectomized rats was higher than that of the intact rats on EG feeding (62.5% vs. 50%), although the difference did not achieve statistical significance. In intact rats fed EG, three of eight (37.5%) showed massive (grade 3) crystal deposits, two of eight (25%) showed moderate (grade 2) crystal deposits, one of eight (12.5%) exhibited mild (grade 1) crystal deposits, and the remaining two of eight (25%) had no crystal deposits. In the

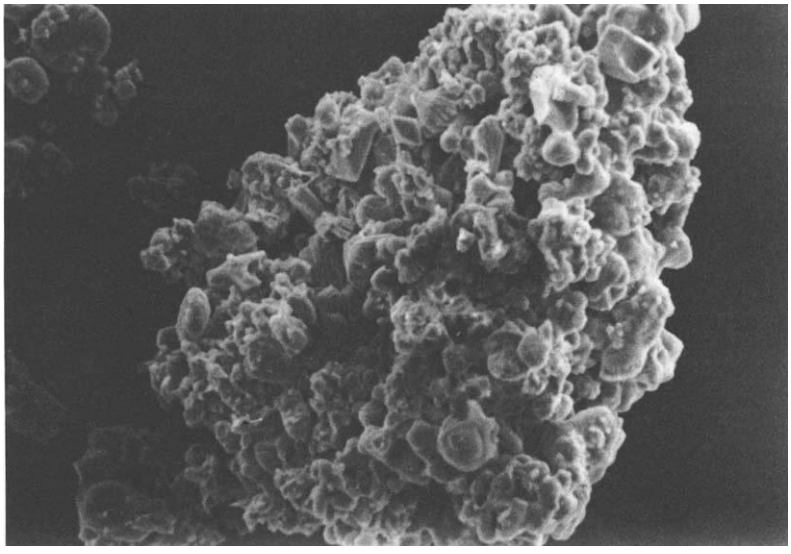

Fig. 6. *Photograph by scanning electron microscopy (SEM).* The SEM revealed aggregates of dumbell and tetragonal-bipyramidal shape crystals indicating calcium oxalate monohydrate and calcium oxalate dihydrate stone, respectively (× 300).

uninephrectomized rats fed with EG, seven of eight (87.5%) showed massive crystal deposits, and one of eight (12.5%) exhibited moderate crystal deposition. Obviously, the uninephrectomized rats had a significantly higher tendency to develop massive crystal deposit than intact rats when fed with EG diet (87.5% vs. 37.5%, $P < 0.05$). The mean stone size was 3.6 mm (range 1.5 to 6 mm). Of the nine urinary stones, six stones (66.7%) were found within the renal pelvis and three stones (33.3%) developed on the renal papilla (Fig. 5). All the stones examined by scanning electron microscopy showed the presence of calcium oxalate (Fig. 6) as has been previously found [18, 19].

Discussion

The ethylene glycol-induced calcium oxalate urolithiasis model in rats has been characterized and extensively used in the study of the mechanism, therapy and prevention of stone formation [12–16, 18, 19]. By using this urolithiasis rat model, the present study aimed to evaluate the potential impact of uninephrectomy on the incidence of urolithiasis in the remnant kidney. Our results indicate that ethylene glycol feeding produced renal crystal deposition in 75% of the intact rats and in all of the uninephrectomized rats. The grade of calcium oxalate crystal deposition in the intact rats ranged from mild (grade 1) to massive (grade 3), whereas the extent of crystal deposition in the uninephrectomized rats was always severe, ranging from grade 2 to 3 (Table 5). The incidence of massive crystal deposition was significantly higher in the uninephrectomized rats than in the intact rats, while that of urinary stone formation was slightly higher in the uninephrectomized rats (63%) than the intact rats (50%), although the difference did not achieve statistical significance. These findings indicate that in the presence of lithogenic risk factors (in this case ethylene glycol), nephrectomy substantially enhances the pathogenesis of renal crystal deposit and urinary stone in the remaining solitary kidney.

Type I distal renal tubular acidosis can induce nephrolithiasis and nephrocalcinosis [20, 21]. In the present study we found that the ethylene glycol treated, uninephrectomized rats had alkaline urinary pH, hypocitraturia, nephrolithiasis and calcium oxalate crystal deposition. These observations suggest that the alkaline urinary pH and hypocitraturia are not the primary cause of urinary calculi formation, but rather the consequence of ethylene glycol feeding and renal damage. Thus, renal tubular acidosis is probably not responsible for the urinary calculi formation in the uninephrectomized rats.

It is well recognized that a reduction in functioning renal tissue is usually followed by adaptive hypertrophy in the structure and function of the residual nephron units that serve to minimize the disturbance of salt and water balance [1–7]. Clinically, the survival rate of patients after uninephrectomy for benign disease is equal to that of normal subjects [22]. Although mild proteinuria and hypertension have been reported in some uninephrectomized subjects [23, 24], the surgery did not decrease the chance of survival [25]. In rats, renal function usually returns to normal within two to three weeks of uninephrectomy [1]. The present results are in accord with previous studies [8, 9], since they show that the renal clearance of creatinine and the excretory function of the uninephrectomized rats fed the normal diet (including those rats subjected to subsequent treatment with ethylene glycol) did not differ significantly from those of control rats. Ethylene glycol feeding was therefore initiated two weeks after uninephrectomy. As shown in Tables 1 and 2, ethylene glycol feeding markedly increased the wet and dry kidney weight of uninephrectomized rats, and the kidney weight was proportionately correlated with the renal calcium content. The more severe the degree of crystal deposition and stone formation, the higher the calcium content of the kidney. Apparently, the increase of kidney weight of the ethylene glycol-treated uninephrectomized rats reflected not only the compensatory renal growth, but also the urinary calculi formation and calcium oxalate crystal deposition. In the rats challenged with the lithogenic diet, there were significant increases in the urinary pH, oxalate excretion and calcium content of the dry kidney tissue, and decreases in calcium excretion and creatinine clearance. These alterations in renal function were

accompanied by a significant decrease in functional kidney parenchyma and an increase in calcium content in the dry kidney tissue and a high incidence of calcium oxalate crystal deposition and urinary stone formation as well. These commonly accepted determinants of urolithiasis were even more striking in the remaining kidney of the uninephrectomized rats (group 4). These data suggest that under circumstances of high risk, such as ethylene glycol feeding leading to uninephrectomy, a compensatory increase in the excretion of lithogenic substances which renders the ipsilateral remnant kidney were vulnerable to crystal deposition and urinary stone formation. Accordingly, the functional compensatory adaptation paradoxically induces both beneficial and adverse effects on the residual kidney, that is, preservation of body fluid homeostasis and increased susceptibility to urolithiasis.

It must be pointed out that a severely compromised renal function, as reflected by a significant increase in serum creatinine and a decrease in creatinine clearance, as well as excretion of sodium, potassium and chloride, occurred simultaneously with renal crystal deposition and urinary stone formation in the remnant kidney. This has significant clinical implications. Some patients seeking medical treatment for stones in one kidney already exhibit severe renal damage in the ipsilateral kidney [26]. The diseased kidney may be either left alone or may require surgical removal later. If urolithiasis patients, who have undergone uninephrectomy or whose unilateral kidney has lost its function, continue to be exposed to dietary and/or other lithogenic risk factors, the remnant kidney may carry a higher risk of stone formation and is therefore more prone to further damage. On the other hand, although the urinary calculi can be removed effectively and safely now by the newly developed methods such as extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy, and rigid and flexible ureteroscopy, if we neglect the preventive measures of urolithiasis patients, 50 to 70% of the stones will recur after treatment [27]. Despite the fact that ESWL is generally considered a safe procedure to treat urinary calculi, some studies demonstrated that ESWL caused significant reductions in effective renal plasma flow (5%), glomerular filtration rate (8%), and morphological changes in the treated kidney [28–34]. Thus, in some recurrent stone formers, especially young ones, repeated ESWL may cause damage to the treated kidney, which has possible ramifications for the other kidney; it may now start forming stones and thereby compromise an already reduced renal function. Nevertheless, a prospective and long-term follow-up study in humans is necessary for clarifying these potentially significant complications.

In summary, ethylene glycol feeding in the intact rats induced renal crystal deposit and urinary stone formation with the incidence of 75% and 50%, respectively. Uninephrectomy alone neither affected the renal function, nor produced urolithiasis and crystal deposition in the remaining kidney. However, ethylene glycol feeding in the uninephrectomized rats significantly increased the incidence (100%) and the severity of calcium oxalate crystal deposition in the remnant kidney. Also, the incidence of urolithiasis increased to 63%, and this was accompanied by a severely compromised renal function in the uninephrectomized rats treated with the lithogenic diet. These data indicate that uninephrectomy renders the remaining solitary kidney more vulnerable to urolithiasis in the presence of lithogenic risk factors.

Acknowledgments

This work was supported by a grant from the Institute of Biomedical Sciences, Academia Sinica, Republic of China to Luke S. Chang. The authors thank Ms. Chao-Chen Lee for her technical assistance.

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